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June 4, 1999

Dockets Management Branch
(HFA-305), Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852.

Re: Medical Devices; Sunlamp Products Performance Standard; Request for Comments and Information

Dear Sirs:

Thank you for extending the time for comments to your Advance Notice of Proposed Rulemaking. As a concerned citizen, I have two comments regarding the performance standards for sunlamp products. Also, I have enclosed an improved version of a manuscript that has been submitted for publication to *Photodermatology, Photoimmunology, and Photomedicine*. I submitted an earlier version for your review.

First, the FDA published the Final Monograph for Sunscreens (Federal Register **64**(1999)27666-27693). In the agency's conclusions on the comments, the agency addressed a comment regarding the definition of UVB. The comment noted that the agency's definition of UVB, 290 nm to 320 nm, differed from that of the Commission International de L'Eclairage (CIE), 280 nm to 320 nm. The agency decided that because the comment did not provide a compelling reason to change to 280 nm for the short-wavelength boundary, the agency will continue to define the boundaries of UVB radiation as 290 nm to 320 nm.

The boundary for UVB defined in the sunscreen Final Monograph differs from the boundary defined for sunlamp products, 260 nm to 320 nm. I request that the agency be consistent with a definition for UVB. If the agency is willing to use a consistent definition of UVB, then some parts of the agency will have to change their definition of UVB. Because the some areas of the agency will have to change, I suggest that the agency change to adopt the definition of the Commission International de L'Eclairage.

Second, the Final Monograph for Sunscreens (Federal Register **64**(1999)27666-27693) defined suntanning preparations (21 CFR 740.19) as preparations "including gels, creams, liquids, and other topical products that are intended to provide cosmetic effects on the skin while tanning through exposure to UV radiation." Further, the agency considers suntanning products to be "intended for repeated use under the sun or suntanning lamps while acquiring a tan" (Federal Register **64**(1999)27669).

However, I believe suntanning preparations used under suntanning lamps should be considered medical devices and regulated as medical devices by CDRH. Products intended for use with medical devices should not be regulated by CDER, as they are attempting through the Sunscreen Final Monograph. For example, ultrasound equipment is a medical device; ultrasound gel, a simple gel formulation, is used with the medical device and must receive favorable review from CDRH prior to marketing.

CDRH best understands the requirements for accessory products to be used with a medical device. All suntanning preparations to be used in conjunction with a tanning bed should receive favorable review from CDRH prior to marketing through either a PMA or through a 510(k). Suntanning preparations to be used with a tanning bed should exhibit characteristics specific for use in a tanning bed. For example, suntanning preparations for use with a tanning bed should:

- be proven to avoid damaging or aging acrylic shields on the tanning bed.
- be proven to be safe in a photoallergic contact dermatitis test on at least 25 subjects.
- contain labeling specific for tanning bed consumers.
- have all claims for safety and for efficacy reviewed by CDRH for accuracy.
- be manufactured in a facility licensed for medical device manufacturing.

I appreciate the opportunity to comment during the rulemaking process.

Sincerely,

/M Caswell

Michael Caswell, Ph.D.
Enc.

The Kinetics of the Tanning Response to Tanning Bed Exposures

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Abstract

No clinical studies have been published documenting the development of pigmentation following the use of FDA recommended exposures from a tanning bed. Panelists were exposed three times weekly for eight weeks (24 exposures) using the FDA recommended exposure schedule. The initial tan was noted after only six exposures and quantitatively increased through the remainder of the study.

Key words: tanning bed, skin, erythema, tan, ultraviolet radiation

Introduction

Although tanning beds are medical devices, the only published study on the development of a tan from a tanning bed was an abbreviated study by Devgun, et al (1) published 16 years ago. The authors reported that most subjects developed a tan after ten exposures over a two-week period. I have examined the development of a tan from a tanning bed for three reasons. First, tanning bed technology has dramatically improved since their study. Second, the authors did not use the FDA recommended exposure schedule. Third, the authors failed to publish an emission spectrum of the bed's ultraviolet radiation.

Herein are the results of a clinical study examining the kinetics of the tanning response to tanning bed exposures over eight weeks (24 exposures) using the FDA recommended exposure schedule. The data suggest that under the conditions detailed in this work, a tan becomes apparent after only two weeks (six exposures).

Materials and Methods

Ultraviolet Radiation Source: This study employed two Wolff System Indoor Tanning System Sundash Gold R-32B (Sun Industries, Inc., Jonesboro, AR) tanning beds. The Sundash R-32B uses 32 Bellarium SA1-10-100W lamps (Wolff Systems Technology, Atlanta, GA) and conforms to CFR21 Part 1040.20. The spectral output of each bed (Rapid Precision Testing Laboratories, Cordova, TN) is displayed in Figure 1. To ensure consistent radiation, intensity and uniformity measurements were taken before each exposure session using an IL700 Research Radiometer. The recommended exposure schedule (Table I) was based on the output of the beds and on each subject's Fitzpatrick skin type.

Biophysical Measurements: Color changes in skin were quantitated with a Minolta Chromameter CR-300 which measures color in the L*, a*, and b* vector system (2-3). Changes in color were quantitated using ΔE (4), where:

$$\Delta E = \sqrt{(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2}$$

Subjects: Three male and 11 female subjects between the ages of 18 and 42 were entered into the study on the basis of three inclusion and eleven exclusion criteria (Table II) and after written informed consent was obtained. Eight subjects were Fitzpatrick skin type III (burns moderately, tans gradually), while six were Fitzpatrick skin type IV (burns minimally, always tans well). Eleven subjects, two males and nine females, completed the study. Three subjects failed to complete the study for reasons unrelated to the study.

Protocol: This study was conducted in a clinical testing laboratory that routinely performs human safety and sunlight efficacy studies. Their technicians are trained to evaluate skin response including erythema and skin pigmentation using standard grading scales.

During a one-week washout period prior to the study and for the remainder of the study, subjects used the shower gel provided for them. Each subject was pre-screened to determine his minimal erythema dose (MED). The MED was determined for each subject by exposing unprotected, naive skin to a series of five ultraviolet radiation exposures each 25% greater than the previous dose. Approximately 24 hours after the exposures, the sites were visually evaluated for erythema illuminated by a 100-watt incandescent blue bulb. The site that produced erythema to the borders of the exposure site using the smallest dose of energy is the subject's inherent MED.

Each subject had one 4cm x 3cm site marked with gentian violet on each side of the spine midway down the back. During irradiations, subjects were clothed except for these two sites. Each subject wore protective eyeware during irradiation. On Visit 1, baseline measurements consisting of visual erythema and visual tanning along with Minolta Chromameter CR-300 measurements were carried out on each site. After these measurements were taken, subjects reclined on the tanning bed acrylic surface and were covered with black felt to prevent stray irradiation from reaching the skin. The top portion of the bed was lowered to irradiate the sites on the back; the bottom set of bulbs were off. After a standard exposure time (Table I), the subject arose from the bed, waited approximately 15 minutes at room temperature, and then had visual and instrumental measurements conducted again.

Evaluations: Test sites on the back of each subject were evaluated visually using a 100 watt incandescent blue bulb for presence and degree of erythema and tan coloration. Skin sites were evaluated by trained technicians at the onset of the study and before and after each treatment. Instrumentally, skin color change was monitored with a Minolta Chromameter CR-300. The scorer remained blinded throughout the study regarding treatment assignments.

The following scoring scales were used for visually evaluating the erythema and tanning of the irradiated sites in relation to the unirradiated control sites.

Erythema		Tanning	
0	No erythema present	0	No difference from untreated control
0.5	Barely perceptible erythema	0.5	Barely perceptible tan coloration
1	Mild erythema	1	Slight tan coloration
2	Moderate erythema	2	Definite tan coloration
3	Strong erythema	3	Dark tan coloration

No adverse event occurred during the course of this study.

Statistical Analysis: The data from all subjects were grouped because no significant differences between Fitzpatrick skin types III and IV were observed. The analysis of variance (ANOVA) with repeated measures due to multiple evaluation times was used to test for statistically significant differences between the two treatments ($p \leq 0.05$). A significant tan or significant erythema is defined as a difference between mean values for the irradiated site and the control site using ANOVA with $p \leq 0.05$.

Results and Discussion

This study is the first to document the kinetics of the tanning response induced by exposure to ultraviolet radiation from a tanning bed. Subjects were exposed to ultraviolet radiation three times weekly for eight weeks (24 exposures). Both 15 minutes before and 15 minutes after each exposure the development of the tan was followed instrumentally (ΔE) and visually by trained technicians and compared to the control site.

The kinetics of the tanning response from repeated exposures to tanning bed ultraviolet radiation.

The development of the tan as assessed instrumentally closely paralleled the development of the tan as assessed visually by trained technicians. Instrumentally, a significant tan after exposure appeared on day 12, at visit 6, and increased steadily thereafter (Figure 2). A significant tan before exposure appeared on day 22, at visit 10, and increased steadily thereafter (Figure 3). Visually, a significant tan after exposure appeared on day 15, at visit 7, and increased steadily thereafter (Figure 2). A significant tan before exposure appeared on day 17, at visit 8, and increased steadily thereafter (Figure 3). After eight weeks (24 exposures) the tan was continuing to increase (Figures 3 and 4). This result shows that UV-radiation from a tanning bed can induce tanning in this population.

The mean of the instrumentally evaluated tan (ΔE) continued to increase over the course of the study. On the final visit, the mean difference between the irradiated and control sites before irradiation maximized at 7.66 Chromameter units and after irradiation maximized at 9.24 Chromameter units. This difference may be due to immediate pigment darkening and persistent pigment darkening. No tanning plateau was reached during the course of this study.

The development of erythema from repeated exposures to tanning bed radiation.

FDA guidelines (CFR21 Part1040) for tanning bed exposure (Table I) were followed. Both 15 minutes before and 15 minutes after each exposure skin redness was followed instrumentally (a^*) and visually by trained technicians and compared to the control site. Visually, differences in means of redness for

average replicates before exposure become significant only on visits 12, 13 and 14 (Figure 4); differences in means of redness for average replicates after exposure become significant on visits 12-17 (Figure 5). Instrumentally, differences in means of redness (a*) both before (Figure 4) and after (Figure 5) exposure become significant on day 15, at visit 7, and increase slightly thereafter. Because the increase in a* parallels the development of the tan, the increase in a* may be the result of the increase in the tan. A tan is known to contain a red component (5). Although visual assessment found little significant erythema in this study, assessing erythema in the presence of a tan is difficult (5). An improved assessment for the presence of erythema could be obtained by using an instrument designed to evaluate the presence of hemoglobins (5). The development of a tan coupled with slight erythema (if any) suggests that FDA guidelines for tanning bed exposures are appropriate to allow for cosmetic tanning with minimal erythema.

The change in Persistent Pigment Darkening (PPD) as tanning occurs.

Persistent Pigment Darkening (PPD) is the pigment that develops following UVA exposure and persists for several hours; Immediate Pigment Darkening (IPD) is the pigment that develops following UVA exposure and persists for minutes. Most, but not all, of the IPD would be absent by fifteen minutes following UV exposure (6), when we measured skin color. The difference between the skin color before UV exposure and the skin color after UV exposure is due primarily to PPD and partially to IPD. If the PPD changes while tanning increases, then a change in PPD would be apparent over the eight-week study. Statistical analysis of the data (Figure 6) indicate a very slight but statistical significant increase in PPD during the course of the study. It is possible that the partial IPD at fifteen minutes might change in an equal but opposite direction to the PPD at fifteen minutes, causing no apparent change. However, this cancellation of IPD and PPD is unlikely.

Chardon, et al, reported no change in PPD among different Fitzpatrick skin types. While his results suggest that PPD is independent of the amount of constitutive pigmentation (Fitzpatrick skin type), the results reported herein suggest that PPD is slightly dependent of the amount of facultative (tanning) pigmentation. The lack of sensitivity to facultative skin pigment is another reason why PPD is an appropriate marker for UV protection assays.

Conclusions

This report details the development of a tan in a population following exposure to ultraviolet radiation produced by a tanning bed according to the FDA exposure schedule. A significant tan developed after only six visits and continued to increase in intensity over the eight-week exposure schedule. Little erythema was

observed visually or instrumentally. Therefore, the FDA tanning bed exposure schedule allows for tanning without overexposure to ultraviolet radiation.

Acknowledgments

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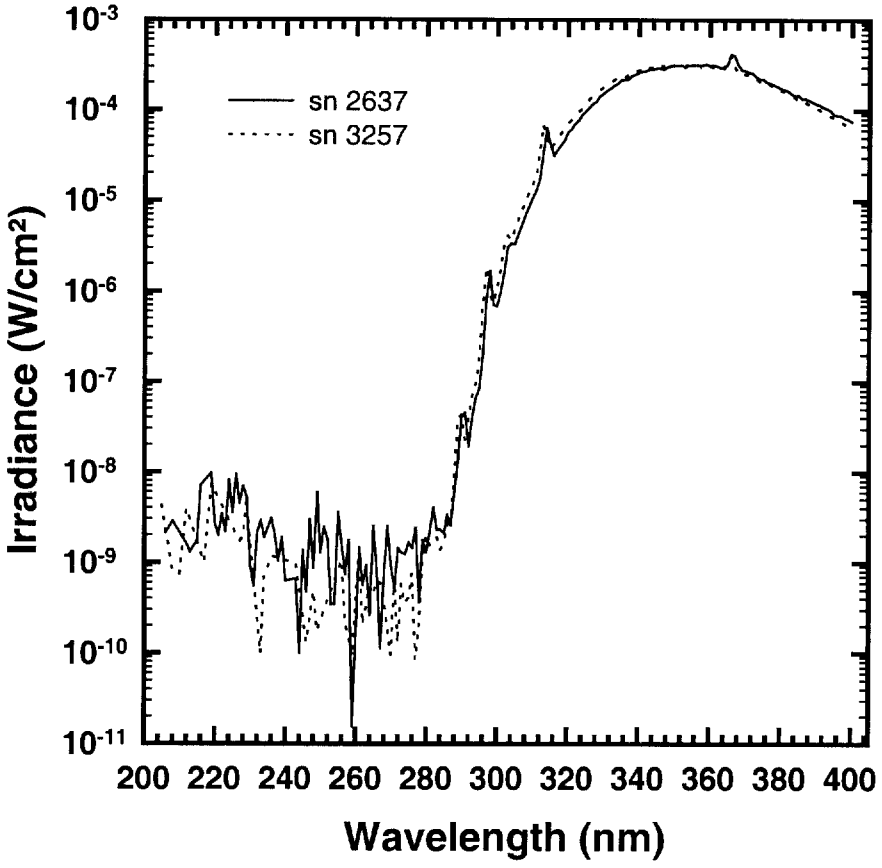

Figure 1. Tanning Bed Emission Spectra. Ultraviolet irradiance of two Wolff System Indoor Tanning System Sundash Gold R-32B (sn 2637 and sn 3257) tanning beds. Spectral output was measured at one nanometer resolution using a calibrated Optronics OL-754 spectroradiometer traceable to NIST (Rapid Precision Testing, Cordova, TN). Each bed contains 32 Bellarium SA1-10-100W lamps and conforms to CFR21 Part 1040.20.

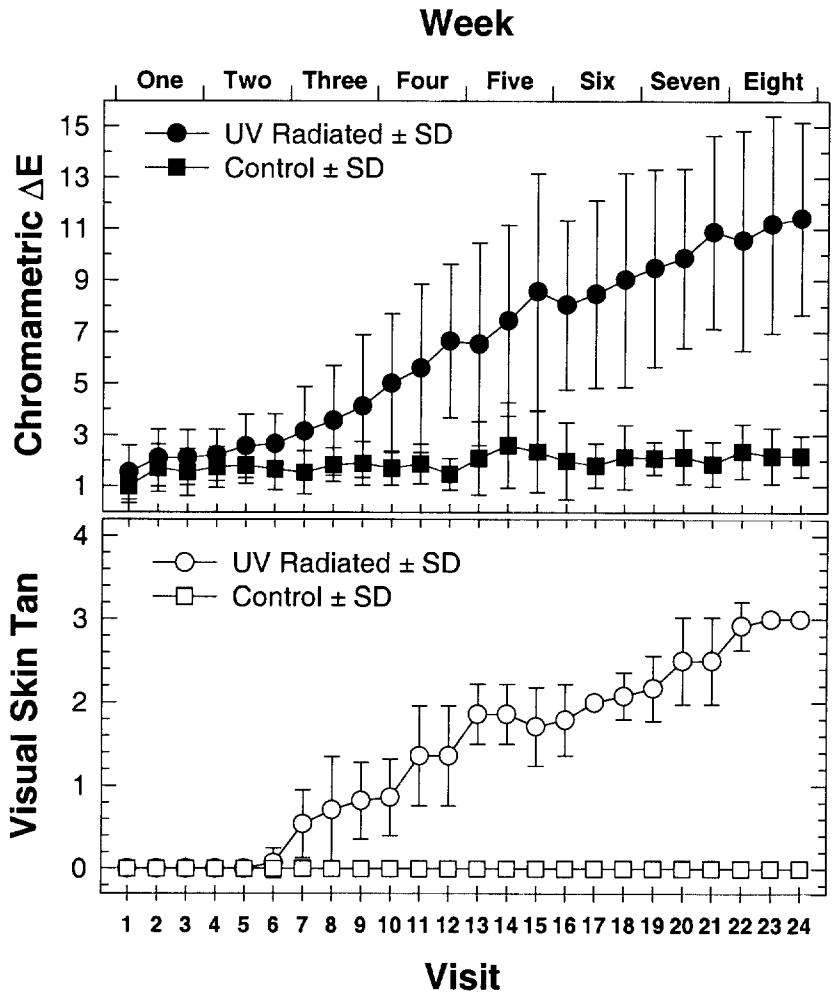

Figure 2. Development of Tan Over Eight Week Schedule. Time course of the change in the mean skin color, ΔE, for the average replicate from baseline **before** irradiation as measured instrumentally with a Minolta Chromameter (upper panel) and visually on a four-point scale (lower panel). The control site shows no significant change in skin color. Only the irradiated site shows a marked increase in skin color, consistent with UV radiation inducing the increase in skin color.

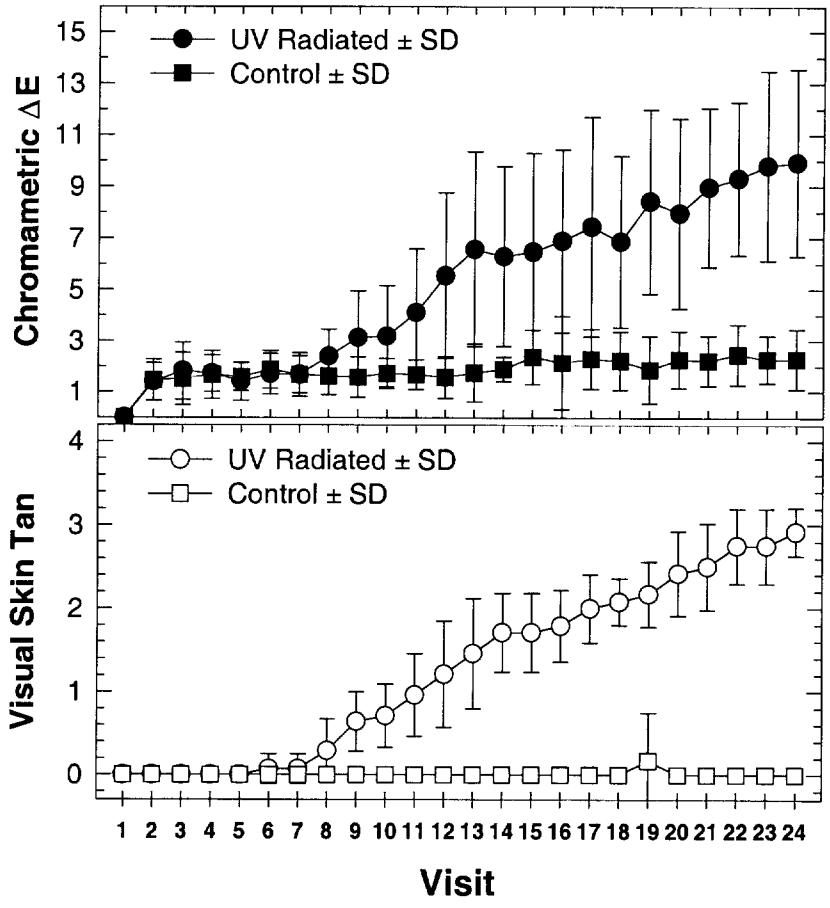

Figure 3. Development of Tan Over Eight Week Schedule. Time course of the change in the mean skin color, ΔE, for the average replicate from baseline **after irradiation** as measured instrumentally with a Minolta Chromameter (upper panel) and visually on a four-point scale (lower panel). The control site shows no significant change in skin color. Only the irradiated site shows a marked increase in skin color, consistent with UV radiation inducing the increase in skin color.

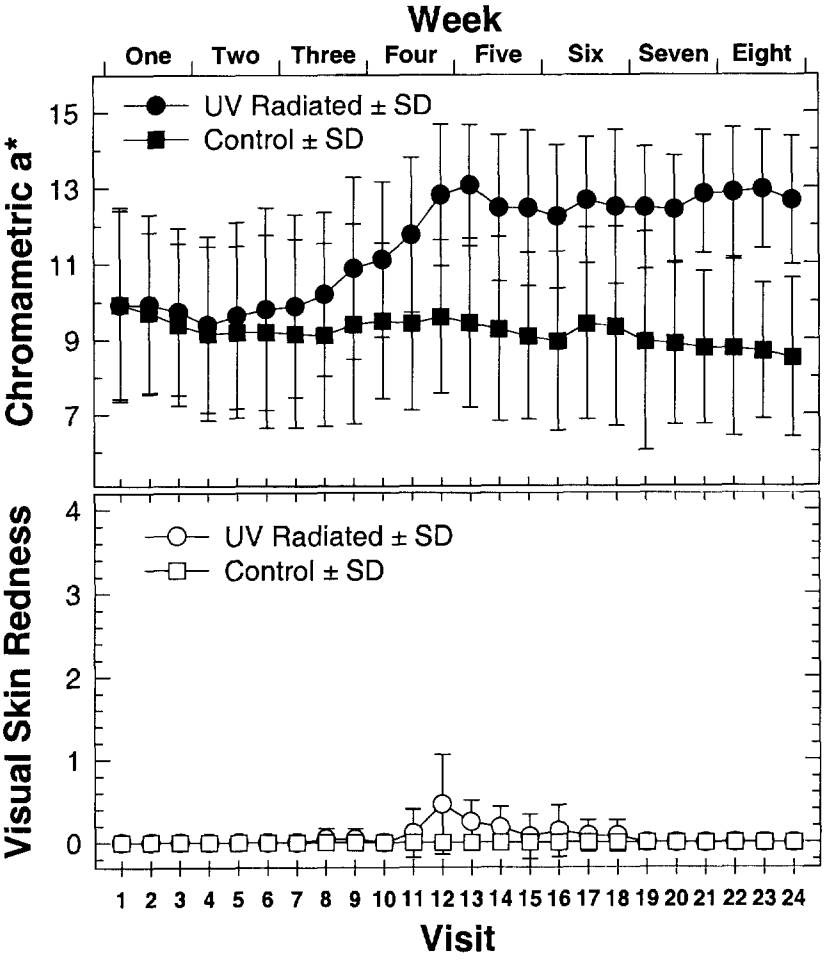

Figure 4. Development of Erythema Over Eight Week Schedule. Time course of the change in the mean red skin color, a*, for the average replicate from baseline **before** irradiation as measured instrumentally with a Minolta Chromameter (upper panel) and visually on a four-point scale (lower panel). The control site shows no significant change in red skin color. Only the irradiated site shows a slight increase in red skin color, consistent with the change being due to overall tanning.

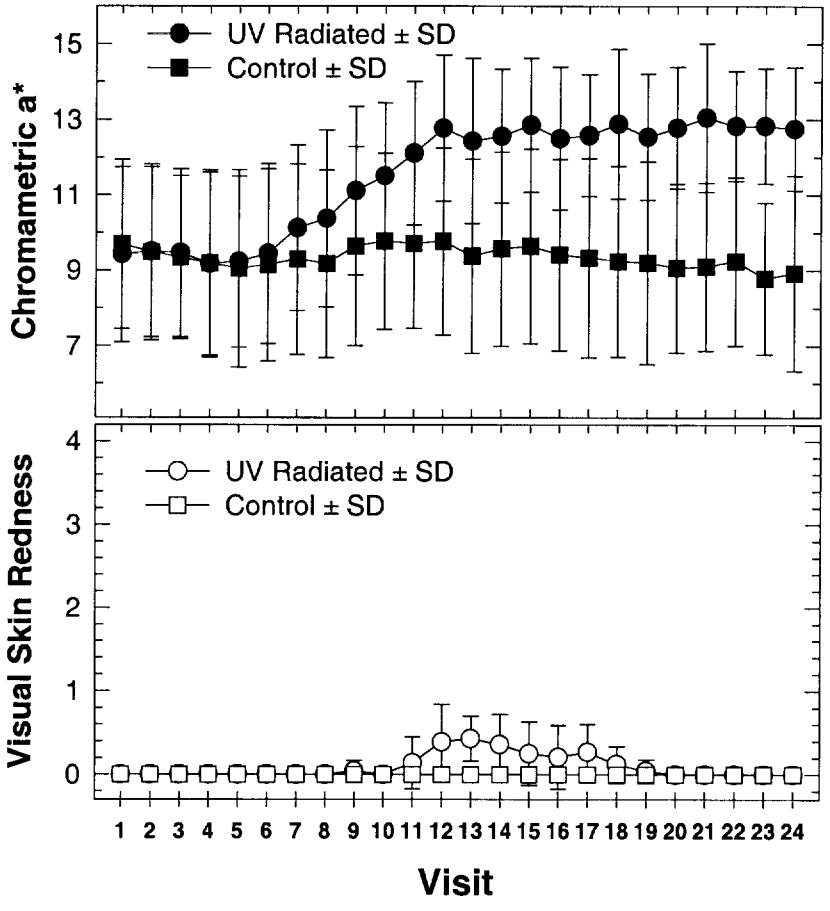

Figure 5. Development of Erythema Over Eight Week Schedule. Time course of the change in the mean red skin color, a*, for the average replicate from baseline **after** irradiation as measured instrumentally with a Minolta Chromameter and visually on a four-point scale. The control site shows no significant change in red skin color. Only the irradiated site shows a slight increase in red skin color, consistent with the change being due to overall tanning.

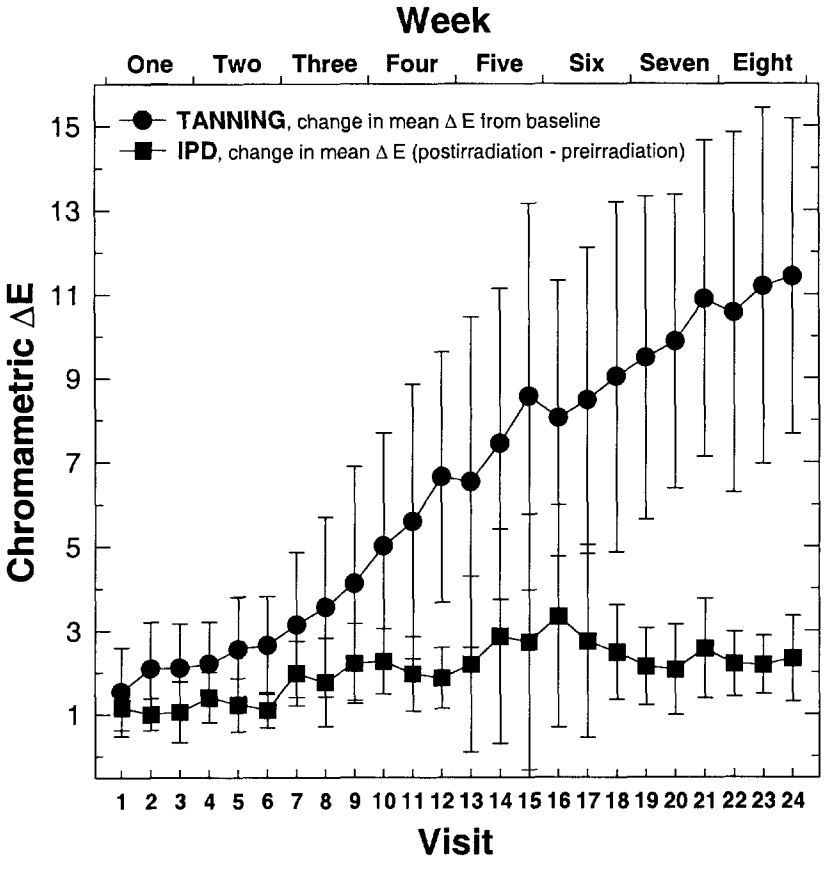

Figure 6. The change in PPD as a tan develops. The upper curve (-●-) indicates the time course of the change in the mean skin color, ΔE, for the average replicate from baseline before irradiation as measured instrumentally with a Minolta Chromameter (same as in Figure 2). The lower curve (-■-) is the difference between after and before means of average replicate from baseline before irradiation as measured instrumentally with a Minolta Chromameter. While the tan increases, the difference between the before and after measurements remains the same, indicating that PPD does not vary with increased tanning.

Table I. Recommended Exposure Schedule

Days	Visit	Week	Skin Type III	Skin Type IV
1, 3, 5	1-3	1	3 min	3 min
8, 10, 12	4-6	2	7 min	10 min
15, 17, 19	7-9	3	15 min	15 min
22, 24, 26	10-12	4	20 min	20 min
29, 31, 33	13-15	5	20 min	20 min
36, 38, 40	16-18	6	25 min	25 min
43, 45, 47	19-21	7	25 min	25 min
50, 52, 54	22-24	8	25 min	25 min

Table II. Exclusion and Inclusion Criteria

Inclusion Criteria

1. Subjects aged 18 to 50 years with Fitzpatrick Skin Type II, III, IV.
2. Subjects in general good health with no active skin disease.
3. Subjects willing to follow study instructions.

Exclusion Criteria

1. Subjects who expect to swim or use sunscreens during the study.
2. Subjects with sensitivities to ultraviolet radiation.
3. Subjects taking drugs known to be photosensitizing.
4. Subjects with clinically significant skin diseases.
5. Subjects who have participated in a photoallergy test or phototoxicity test in the previous 4 weeks.
6. Subjects with routine high dosage use of anti-inflammatory drugs, immunosuppressive drugs, or antihistamine medications.
7. Subjects with immunological disorders.
8. Subjects who are pregnant or lactating.
9. Subjects expecting to unduly expose themselves to sunlight during the course of the study.
10. Subjects who have a condition or are taking medication which places the subject at undue risk.
11. Subjects previously diagnosed with skin cancer.

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